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EXAMINER	
WESSENDORF, TERESA D	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/636,243
Filing Date: August 10, 2000
Appellant(s): WANG ET AL.

Dahna Pasternak
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/23/04 (reinstated as per the request made on 8/8/03) and Supplemental Brief on 8/8/03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

5003

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences, which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

This appeal involves claims 5-6 and 20.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

The amendment after final rejection filed on 5/12/03 has not been entered.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: issue (1) relating to the drawings described in the substitute specification and issue (2) that relate to the unduly confusing substitute specification are petitionable subject matter under 37 CFR 1.181 and not to appealable subject matter. See MPEP §

1002 and § 1201. The 35 USC 102 rejection over Kim is being dropped and therefore longer an issue in the Appeal. Thus, the issues under appeal are 35 USC 112, first paragraph; 35 USC 112, second paragraphs (only with respect to the rejection drawn to the non-naturally occurring peptide linkers) and 35 USC 102 over Pomerantz.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 5-6 and 20 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Pomerantz et al, Structure-based design of a dimeric zinc finger protein, Biochemistry, vol. 37, No. 4, Jan. 1998, pages 965-970.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, first paragraph

Claims 5, 6 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The as-filed specification does not describe a claimed zinc finger complex comprising two or more fusion proteins linked by peptide linkers that are non-naturally occurring peptides. The specification, particularly the Examples, describes a fusion protein of a zinc finger fused to a random peptide library as the non-naturally occurring peptide linker. The peptide obtained from the random library dimerizes into another zinc finger on binding to its DNA target. However, there is no description of two fusion proteins wherein each zinc finger protein is fused separately to each non-natural peptide linker. It is not readily apparent from the disclosure whether a dimerizing peptide is the non-naturally occurring peptide linker. The definition in the disclosure at page 8, lines 5 does not seem to include a dimerizing peptide as a non-naturally occurring peptide linker. It simply recites that some non-naturally occurring sequences are selected from random peptide libraries. There is no description of the kind, length of sequences and/or structural information for the sequences found in nature to preclude the non-naturally occurring linker peptides as per the definition at

page 8, line 5. Furthermore, in a complex of more than two zinc fingers each linked to linkers, there is no description as to which linkers from the multiple ones bound to each zinc fingers the ones that bind specifically to one another. Thus, it is not readily apparent from the specification whether the instantly claimed linker is the linker as generally described in the description section e.g., page 11 or the dimerizing peptide as described in the detailed description of the Examples. See further the RESPONSE below.

Claim Rejections - 35 USC § 112, second paragraph

Claims 5-6 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear within the claimed context as to what constitutes a non-naturally occurring peptide linkers. See further the RESPONSE below.

Claim Rejections - 35 USC § 102

Claims 5 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Pomerantz (Biochemistry).

Pomerantz discloses a zinc finger complex comprising the same zinc fingers 1 and 2 from ZIF 268 with a dimerizing peptide

and linker from GAL4 that forms a dimer with a target. See page 966, Materials and Methods and RESULTS starting at page 967. Therefore, the specific zinc finger protein complex of Pomerantz fully meets the broad scope of the claimed zinc finger complex.

(11) Response to Argument

35 USC § 112, first paragraph

Appellants argue that it is not necessary that the application describe the claimed invention in ipsis verba. Rather, all that is required is that the specification reasonably conveys possession of the invention. In re Lukach, 169 USPQ 795, 796 (CCPA 1971).

Appellants argue that any written description inquiry must begin with claims construction, it is important to note at the outset that the claims on appeal are drawn to complexes that can include multiple zinc finger proteins linked via specific binding of two dimerizing peptide linkers (one or more linkers associated with each fusion protein). Furthermore, each zinc finger protein of the fusion protein components itself contains a plurality of zinc finger components i.e., is a multi-finger (polydactyl) zinc finger protein. Thus, the claims on appeal do not encompass any and all fusion proteins. Appellants rely at page 11,lines 8-14, lines 20-22 and Examples 1 and 2 the description of how a multiple polydactyl zinc finger proteins

are linked using non-naturally occurring dimerizing peptides. Appellants further quote page 12, lines 20-23 and page 13, lines 22-34 of the specification.

In reply, the claims do not recite a multiple zinc finger proteins linked via ***specific binding of two dimerizing peptide linkers (one or more linkers associated with each fusion protein)***. (Note the claim amendment after final filed on 5/12/03, which contains this limitation was not entered.) Rather, a complex formed from a fusion of two zinc finger proteins linked by peptide linkers that specifically bind to each other. The specification, specifically at page 28, Example 1, describes selected variant peptides form the random library that promotes dimerization of the zinc fingers on an appropriate DNA target site. The dimerization occurs between the two fusion proteins of ZIF268 by the 15-mer peptide when the ZiF bind to the DNA target. It does not describe two linkers each linked to each ZIF wherein the linkers specifically binds to each other to form a fusion of two zinc fingers as schematically depicted by appellants at page 9 of the 8/8/03 Brief. It is of interest to note applicants' statement or questions with respect to these dimerizing peptide linkers at page 29, lines 3-8. Appellants state that the selection of dimerization elements from libraries of random peptides represents an ***intriguing*** alternative to

structure-based design and raises many interesting questions. How common are ***functional dimerization units***? Do the selected structures always resemble known motifs? Can we obtain new dimerization units that would be useful when designing transcription factors for potential applications in general therapy? Thus, the dimerizing peptide linkers appear to be of a different concept from that of the (covalent?) linker as presently claimed. Notwithstanding this, the multiple zinc finger encompasses a huge scope of different zinc finger proteins, as well. The specification at paragraph bridging pages 7 and 8 defines in numerous way a zinc finger DNA binding protein as (1) a protein or segment within a larger protein that binds DNA in a sequence-specific manner. (2). A designed zinc finger protein is a protein not occurring in nature whose design/composition results principally from rational criteria. Rational criteria for design include application of substitution rules and computerized algorithms for processing information in a database storing information of existing ZFP designs and binding data. (3). A selected zinc finger protein is a protein not found in nature whose production results primarily from an empirical process such as phage display. Furthermore, pages 16-17 appellants list some of these zinc finger proteins and provide a certain rules for mutation of the zinc finger protein.

The assumption underlying the rules, namely that a particular amino acid in a zinc finger is responsible for binding to a particular base in a subsite is only approximate. Thus, at the time of filing, appellants are deemed to have no possession of the present claims as the specification provides confusing, and at times, conflicting statements or showing as to what is included or precluded by the claimed genus.

A review of page 11, lines 8-11 of the disclosure, as cited by appellants above, is directed to a GENERAL DESCRIPTION. It states methods for selecting dimerization peptides that mediate association of linked functional proteins domains. The peptides can mediate such association by homodimerizing with each other, by heterodimerizing with the linked protein domains, or by binding to an entity, such as a DNA target site, itself bound by the linked protein domains. In particular, such peptides are useful for mediating association of complexes of multiple zinc finger proteins the thereby affording greater specificity and/or affinity in binding of the zinc finger proteins to proximately spaced target segments .. This general statement does not appear to be in consonant with the detailed description given in the Examples. Example 1 at page 28 provides a description of a fusion between the single zinc finger Zif268 and a peptide linked to the N-terminus of said

ZIF268 via random phage display of random sequences of 15-residue polypeptides. And reoptimization of the peptides to further stabilized the protein-DNA complex. Biochemical experiments confirmed that the selected peptides promote dimerization of the zinc fingers on an appropriate DNA target site. The affinity and specificity of DNA-binding proteins (e.g., Zinc finger) depend not only on interactions with the DNA but also on interactions with proteins that bind at neighboring sites. Such protein-protein interactions may involve homo-or heterodimerization or the assembly of multiprotein complexes. It is not apparent from this description whether a random peptide is used to form two linkers that link to two different or separate zinc fingers, let alone to more than two linkers and zinc fingers. Thus, the claimed peptide linkers each linked to a zinc finger protein that specifically bind to each other appears to be of different concept than the dimerizing peptide linker. (The claims appear to recite a covalent linking peptide). The definition of non-naturally occurring peptide linkers provide for more confusion rather than clarification of the claimed invention. (See the definition quoted by appellants below.)

Appellants, at the time of filing, does not show that the invention was complete by describing distinguishing identifying

characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). The knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the numerous general statements (at times are more confusing) in the specification.

35 USC 112, second paragraph

Appellants argue that the term non-naturally occurring is defined beginning on line 3 of page 8 to include only those sequences not found in nature . Additional metes and bounds are also set forth in the this paragraph:

> Conversely, the term non-naturally occurring is used to describe objects and sequences not found in nature. Preferred non-naturally occurring sequences show no significant sequence identity e.g., less than 50% (amino acid or nucleotide) with natural sequences, in distinction from induced mutations of natural sequences. Typically, non-naturally occurring sequences do not contain a contiguous segment of at least half their length with a natural protein. Some non-naturally occurring peptides fold in conformations distinct from natural peptides. Some non-naturally occurring sequences are selected from random peptide libraries.

In other words, the specification plainly defines what is included or excluded from by the recitation non-naturally occurring as naturally occurring linker sequences are clearly excluded from the scope of the pending claims. Thus, when properly read in light of the specification, claim 5 reasonably apprises those skilled in the art as to the metes and bounds of the claimed subject matter and is more than sufficiently precise.

In reply, the negative limitation that is it not found in nature simply recites what is the obvious. Its definition of no significant sequence identity e.g., less than 50% amino acid appear to go against the conventional wisdom of the art of induced mutations of the natural sequence, e.g., as the instant random peptide libraries. Furthermore, to define a non-naturally occurring peptide by its folding conformation is confusing without reciting a structure for said peptide. The primary structure of a peptide has to be given before its folding conformation can be determined. The exemplified peptide from the random peptide given in the specification is not described to fold conformation distinct from the natural sequence. [An appellant may be his own lexicographer however; he cannot go against what is commonly used in the art. Also, the patentee is

permitted to be his own lexicographer carries with it the connotation that he will use terms consistently throughout his patent . See Porter v. Farmers Supply Services Inc. 228,USPQ 4 and see 221 USPQ 1025, 1031]. W

35 USC 102

At the outset, appellants assumption that the Pomerantz(Biochemistry) cited as reference AP-1 in the IDS of 7/6/2001 used in the rejection is correct (as evident from the cited page 967).

Appellants argue that the dimerizing linker used by Pomerantz, namely amino acids 41 to 100 of GAL4, is clearly a naturally occurring sequence, inasmuch as it is part of the naturally occurring GAL4 protein. Appellants further argue that the fact that Pomerantz successfully used naturally occurring sequences as dimerization domains provides no motivation to explore the use of non-naturally-occurring peptides as dimerizing linkers.

In response, attention is drawn to the abstract of Pomerantz. Pomerantz recites that a ***portion*** of Gal4 is used as dimerizing linker. This portion is shown at page 967, col. 1 under the heading section RESULTS i.e., the portion that binds to the 13-residue DNA substite. Read in the light of the specification definition of a non-naturally occurring peptide

linkers ***e.g.***, less than 50% (amino acid) with natural sequences the GAL4 (41-100 residues) is less than 50% of the naturally occurring sequence of Gal. Furthermore, the rejection is an anticipation rejection not an obviousness rejection; hence, no motivation is required.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,
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